REMARKS

1. Please enter the new claims 43-45 for further consideration.

2. Caplan taught that "the human bone marrow is then transferred to a 50 ml centrifuge tube and centrifuged at low speed to yield a cell pellet. Fat and plasma are removed from the centrifuge tube by aspiration.isolation. ...The human bone marrow sample is then concentrated to remove plasma and cleared of red blood cells either by NH_4Cl treatment as described above or by passage of the samples over a Leukosorb™ filter contained in a syringe cartridge filter removing fat, red blood cells and plasma." (Example 6 of US patent 5811094).

There is no finding that one of ordinary skill in the art could modify Caplan's disclosure in the way of this application. One of ordinary skill in the art would not have recognized that the results of the combination of Caplan, Matsui and Prockop were predictable. Indeed, there is no finding to support the combination would improve the culture efficiency.

3. Matsui's disclosue (US patent 4871674) was critized to be "In the use of these cell culture inserts, gases may not be exchanged sufficiently because the area between the sidewall of the insert and the culture plate is too small." (Column 1, line 37 to 39 US patent 5652142). One of the ordinary skill in the art would also run into difficulty to adopt Matsui's device as the upper plate of this application.

4. The specification of Prockop (US patent 7374937) clearly disclosed that "However, prior art methods for isolating MSCs and inducing their proliferation have practical limitations, including the extent of population expansion that can be achieved using prior art methods. There remains a critical need for methods of reliably inducing significant proliferation of MSCs in culture without inducing differentiation of the MSCs as they proliferate." Column 5, line 21 to line 28

Prockop's disclosure was quietly close to that of this application, which would present the status of art in the year of 2000. Professor Prockop is a one of the major players in the field and failed to develop the method disclosed in this application. It would be one of strong evidences that "one of ordinary skill in the art could not have combined the claimed elements by known methods (e.g., due to technological difficulties)" MPEP 2141

Furthermore, this application also demonstrated that "In one preferred embodiment of the present invention, the isolated MSCs proliferate without differentiation and reach confluence even after 12 passages. The cell populations having greater than 98% homogeneous MSCs are obtained in accordance with the method of the present invention." [0031] of this application. The evidence demonstrated the "the results of the claimed combination were unexpected." MPEP 2141

If one of ordinary skill in the art had recognized that the unexpected results, as we disclosed in this application, she/he would have used such a method. It is not persuasive or even impossible for one of ordinary skill in the art to recognize the combination as described in this application, but a major player, such as Professor Prockop, failed to do so.

In the really world, the US patent 7374937 has not been disclosed until May 20, 2008. Indeed, no finding can be articulated for one of the ordinary skill in the art to do the combination.

No finding supports that one of the ordinary skill in the art or even the major players in the art would do the combination. Furthermore, the results of this application were unexpected. Therefore, the rejection of claim 1 under §103 should be withdrawn.

5. Regarding the claims of this application rejection under 35 U.S.C. 103(a) as being unpatentable over Caplan et al in view of Burkitt et al and Mussi et al, Burkitt et al taught red blood cells are 6.7-7.7 μ m diameter and nucleated cells have a diameter greater than 7.7 μ m in 1993. However, Caplan clearly disclosed that "As a whole, bone marrow is a complex tissue comprised of hematopoietic stem cells, red and white blood cells and their precursors, mesenchymal stem cells, stromal cells and their precursors, and a group of cells including fibroblasts, reticulocytes, adipocytes, and endothelial cells which form a connective tissue network called "stroma". (Column 7, line 12-16, US Patent 5811094) The red blood cell is only one of the components in bone marrow. The Caplan's US Patent 5811094 was issued on September 22, 1998. Up to the date of this application, there was no finding between these 12 years to support that one for the ordinary skill in the art would do the modification. Further, the difficulty, mentioned above, of using Matsui's device would also teach away the modification.

6. Regarding the claims of this application rejection under 35 U.S.C. 103(a) as being unpatentable over Caplan et al in view of Guirguis and Mussi et al, Guirguis disclosed "An apparatus for collecting biological fluids and holding samples taken from a biological fluid for qualitative and quantitative testing." (Abstract, US patent 5077012) No funding supports that one of ordinate skill in the art of stem cell would refer to the disclosure of Guirguis, which is "an apparatus for detecting disease markers both for screening as well as for a reference laboratory setting." (Column, 1 line 15 to line 17) These two fields are indeed different. Furthermore, up to the date of this application, there was no finding between these 12 years to suuport that one for the ordinary skill in the art would modify Caplan's disclosure in view of Guirguis and Matsui. Of course, the difficulty of using Matsui's device would also support no such a modification.

7. This application disclosed that "in one preferred embodiment of the present invention, the isolated mesenchymal stem cells proliferate without differentiation and reach confluence even after 12 passages. The cell populations having greater than 98% homogeneous MSCs are obtained in accordance with the method of the present invention."[0031] This application adds these "unexpected results" in claims 43-45. (MPEP 2145 & 716.02) The unexpected results were supported by post-filling art (Kato et al US Patent Application 20050013804, filing date: 09/12/2001), which mentioned that "The conventional culture methods however cannot produce sufficient amounts of mesenchymal stem cells because the proliferation of said stem cells stops or becomes extremely slow around 15th generation."

Accordingly, this application should be placed in condition of allowance. An early Notice to this effect is respectfully expected.

Respectfully submitted:
By: Shih-Chieh Hung

Shih-Chieh Hung
886-2-28757557 ext 118 (voice)
886-2-28265164 (fax)
hungsc@vghtpe.gov.tw(email)
No 201 Shih-Pai Rd Section II,
Taipei-Veterans General Hospital, Taipei,
Taiwan, R. O. C.